BIRTH DEFECT RISK FACTOR SERIES: GASTROSCHISIS

DEFINITION

Gastroschisis is an abdominal wall defect involving herniation of the intestines and sometimes the liver outside of the abdomen. The defect occurs lateral to the umbilicus, usually on the right, and never includes a covering sac. The defect may be confused with other abdominal wall defects such as omphalocele and body stalk anomaly. Infants with gastroschisis tend to have fewer additional birth defects, including chromosomal abnormalities, and a higher survival rate than other abdominal wall defects, particularly omphalocele (Barisic et al., 2001; Forrester and Merz, 1999a; Rankin et al., 1999; Tan et al.,1996; Calzolari et al., 1995; Morrow et al., 1993; Torfs et al., 1990; Roeper et al., 1987; Carpenter et al., 1984; Mann et al., 1984; Bugge and Hauge, 1983; Baird and MacDonald, 1981).

Over the past several decades, women carrying a fetus with gastroschisis have been found to have elevated maternal serum levels of alpha-fetoprotein (Canick and Saller, 1993). Prenatal screening of this substance, along with ultrasonography (Vintzileos et al., 1987), have allowed gastroschisis to be identified in utero. Studies from various birth defects surveillance systems have found that, in regions where elective termination is allowed, the birth prevalence of gastroschisis is reduced, although this difference was small compared with other abdominal wall defects (Stoll et al., 2001; Barisic et al., 2001; Forrester and Merz, 1999b; Rankin et al., 1999; Byron-Scott et al., 1998; Riley et al., 1998; Heydanus et al., 1996; Calzolari et al., 1995; Chi et al., 1995; Stoll et al., 1995; Julian-Reynier et al., 1994; Morrow et al., 1993; Stoll et al., 1992).

EMBRYOLOGY

Prior to the tenth week of gestation, the intestine of the fetus herniates into the umbilical stalk. At 10-12 weeks' gestation, the intestine retracts into the abdomen. If this retraction fails to occur, gastroschisis may result. This failure may result from vascular disruption (Hoyme et al., 1983; de Vries, 1980)

DEMOGRAPHIC AND REPRODUCTIVE FACTORS

Several studies have investigated the relationship of **race/ethnicity** to gastroschisis and failed to find any association (Torfs et al., 1994; Yang et al., 1992; Roeper et al., 1987). One study in Hawaii found gastroschisis prevalence to be lower in Far East Asians than whites, Pacific Islanders, and Filipinos; however, this difference disappeared when the rates were adjusted for maternal age (Forrester and Merz, 1999a). Another investigation observed no significant difference in risk of abdominal wall defects in infants born to Vietnamese women compared with infants born to non-Hispanic white women in California (Shaw et al., 2002).

Secular trends have been observed in gastroschisis prevalence since the 1970s. Overall, gastroschisis rates have increased around the world (Bugge and Holm, 2002; Forrester and Merz, 1999a; Rankin et al., 1999; Tan et al., 1996; Roeper et al., 1987; Martinez-Frias et al., 1984; Hemminki et al., 1982), although this trend has not always been noted (Yang et al., 1992; Goldbaum et al., 1990; Carpenter et al., 1984; Bugge and Hauge, 1983; Baird and MacDonald, 1981). At least for some studies examining earlier periods, this trend may be due to misclassification of gastroschisis as other abdominal wall defects in the first part of the interval examined; however, for the studies examining later periods, this is less likely to have been a plausible explanation for the prevalence increase.

Prevalence of gastroschisis shows wide variation by **geographic location**, both within and between

countries (Tan et al., 1996; Goldbaum et al., 1990; Roeper et al., 1987; Hemminki et al., 1982). One investigation failed to identify any association between gastroschisis and **altitude** (Castilla et al., 1999).

Literature that examined **maternal age** risk for gastroschisis found much higher rates for very young mothers (Bugge and Holm, 2002; Barisic et al., 2001; Stoll et al., 2001; Hollier et al., 2000; Forrester and Merz, 1999a; Rankin et al., 1999; Byron-Scott et al., 1998; Calzolari et al., 1995; Haddow et al., 1993; Werler et al., 1992a; Yang et al., 1992; Goldbaum et al., 1990; Torfs et al., 1990; Roeper et al., 1987; Martinez-Frias et al., 1984; Bugge and Hauge,1983; Hemminki et al., 1982). One study identified a decline in gastroschisis risk with increasing **parity**, although this observation was due to confounding by maternal age (Byron-Scott et al., 1998). Other studies found no relationship between gastroschisis rates and parity (Torfs et al., 1994; Roeper et al., 1987). An association of gastroschisis risk with **previous elective terminations** and a **short interval between menarche and first pregnancy** has been reported (Torfs et al., 1994), although one study did not report any link between previous elective terminations and gastroschisis (Werler et al., 1992a). These relationships may reflect either a biological effect or sociodemographic factors.

Infant sex is associated with the risk for gastroschisis. Males are more likely than females to have gastroschisis (Forrester and Merz, 1999a; Riley et al., 1998; Tan et al., 1996; Calzolari et al., 1995; Torfs et al., 1994; Goldbaum et al., 1990; Roeper et al., 1987; Carpenter et al., 1984; Hemminki et al., 1982; Baird and MacDonald, 1981); however, not all studies have reported this association (Stoll et al., 2001). Gastroschisis is also associated with lower **birth weight**, **prematurity**, and **intrauterine growth retardation** but not **plurality** (Rasmussen et al., 2001; Stoll et al., 2001; Riley et al., 1998; Mili et al., 1991; Khoury et al., 1988). However, one study reported increased risk of abdominal wall defects with multiple gestation pregnancy (Mastroiacovo et al., 1999). One investigation reported no statistically significant association between gastroschisis and **macrosomia** (Waller et al., 2001).

There does not appear to be an association between parental **consanguinity** and gastroschisis (Rittler et al., 2001).

FACTORS IN LIFESTYLE OR ENVIRONMENT

Since gastroschisis risk is significantly increased with young maternal age, many studies have investigated factors that may be associated with younger women. Maternal **socioeconomic status** has been found to affect gastroschisis risk. One study reported that demographic variables indicating low socioeconomic status were associated with increased rates of gastroschisis. This included lower levels of **maternal education** and lower **family income** (Torfs et al., 1994). However, another investigation failed to find an association between less than twelve years of education and gastroschisis risk (Werler et al., 1992a). A third study reported an increased risk of abdominal wall defects with socioeconomic deprivation, although the difference was not statistically significant (Vrijheid et al., 2000).

In relation to **maternal occupation**, one study has suggested a link between increased gastroschisis risk and commercial and sales work (Hemminki et al., 1982). Another study found an association between gastroschisis and maternal exposure to **solvents** and **colorants** (Torfs et al., 1996).

Living in proximity to **hazardous waste sites** or various **industries** has not been found to affect risk of gastroschisis (Castilla et al., 2000; Dolk et al., 1998), although one investigation found a slightly increased risk of abdominal wall defects with proximity to **landfill sites** (Elliott et al., 2001). There does not appear to be an association between **parental farming** occupation or **pesticide** exposure and risk of gastroschisis (Kristensen et al., 1997), or **water chlorination** and abdominal wall hernia (Kallen and Robert, 2000).

One study has tentatively suggested that inadequacies in the mother's **diet** may increase risk for gastroschisis (Torfs et al., 1998). Another study found low maternal prepregnancy **body mass index** to

be associated with gastroschisis (Lam 1999). One investigation reported an increased rate of abdominal wall defects among infants born to non-diabetic **obese** women (Moore et al., 2000), while another investigation reported no association between maternal obesity and gastroschisis (Watkins et al., 2001). Maternal **hyperthyroidism** and **hypothyroidism** do not appear to increase risk of gastroschisis (Khoury et al., 1989). One investigation reported no association between maternal **fever**, **upper respiratory infection**, or **allergy** and gastroschisis (Werler et al., 2002).

Women who **smoked** were more likely to have an infant with gastroschisis (Torfs et al., 1994; Haddow et al., 1993; Goldbaum et al., 1990), although not all investigations found this effect (Werler et al., 1992a). Maternal consumption of caffeinated and decaffeinated **coffee** has not been found to increase gastroschisis risk (Werler et al., 1992a). One study reported a potential association between periconceptional **X-ray** exposure and gastroschisis (Torfs et al., 1996). Maternal **alcohol** use has been linked to higher rates of gastroschisis (Torfs et al., 1994; Werler et al., 1992a), as has **recreational drug** use (cocaine, amphetamine, marijuana, or LSD)(Torfs et al., 1994, Drongowski et al., 1991).

The link between maternal **cocaine** use and gastroschisis risk is important because cocaine is a vasoconstrictor. One hypothesis offered for the etiology of gastroschisis is that it is a vascular disruption defect (Hoyme et al., 1983; de Vries, 1980). Further support for this hypothesis is provided by studies that found increased rates of gastroschisis among infants born to mothers who had used the vasoactive medications **salicylates** (**aspirin**), **pseudoephedrine**, **acetaminophen**, and **phenylpropanolamine** (Werler et al., 2002; Martinez-Frias et al., 1997; Torfs et al., 1996; Werler et al., 1992b), although one of these studies found no association between phenylpropanolamine, **ibuprofen**, **antihistamines**, **guaifenesin**, or **dextromethorphan** and gastroschisis (Werler et al., 2002).

In one investigation, **antibiotics**, **antinauseants**, **sulfonamides**, and **oral contraceptives** were not linked to gastroschisis risk (Torfs et al., 1996). Another study reported no association between maternal use of the antibiotic **oxytetracycline** during pregnancy and omphalocele/gastroschisis (Czeizel and Rockenbauer, 2000). Recent investigations found no relationship between **cephalosporin antibiotics**, **nalidixic acid**, **ampicillin**, or the **benzodiazepines** nitrazepam, medazepam, tofisopam, alprazolum, and clonazepam and omphalocele or gastroschisis (Eros et al., 2002; Czeizel et al., 2001a; Czeizel et al., 2001b; Czeizel et al., 2001c). Gastroschisis does not appear to be associated with **misoprostol**, a synthetic prostaglandin used for elective termination (Orioli and Castilla, 2000).

Maternal **folic acid** use does not appear to influence risk of abdominal wall defects (Czeizel et al. et al., 1996). Furthermore, a study that examined **co-trimoxazole**, a combination of trimethoprim and sulfamethoxazole that is a folic acid antagonist, failed to find any association between the medication and abdominal wall defects (Czeizel, 1990).

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Please Note: *The primary purpose of this report is to provide background necessary for conducting cluster investigations. It summarizes literature about risk factors associated with this defect. The strengths and limitations of each reference were not critically examined prior to inclusion in this report. Consumers and professionals using this information are advised to consult the references given for more in-depth information.*

This report is for information purposes only and is not intended to diagnose, cure, mitigate, treat, or prevent disease or other conditions and is not intended to provide a determination or assessment of the state of health. Individuals affected by this condition should consult their physician and when appropriate, seek genetic counseling.